NOT FOR PUBLICATION **FILED UNDER SEAL**

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

ALTANA PHARMA AG and WYETH, Plaintiffs, v. KUDCo, Defendant.	CIVIL ACTION NO. 04-2355 (JLL) **OPINION**

LINARES, District Judge.

This is a patent infringement action to enforce United States Patent No. 4,758,579 ("the '579 patent"). The asserted claims of the '579 patent – claims 22 and 25 – cover a chemical compound named Pantoprazole, and its sodium salt, pantoprazole sodium.[1] Pantoprazole is the active ingredient in PROTONIX®, a drug manufactured for the treatment of gastric acid disorders. Plaintiff Nycomed GmbH (formerly known as Altana Pharma AG and, at the time of the invention, Byk Gulden) owns the '579 patent. Plaintiff Wyeth markets and sells Protonix in the United States as Nycomed's exclusive licensee.[2]

Defendant KUDCo ("Defendant" or "KUDCo") filed an Abbreviated New Drug Application ("ANDA") with the United States Food and Drug Administration to market and sell a generic version of Protonix in the United States. KUDCo stipulated that it has infringed the asserted claims if those claims are valid and enforceable. However, KUDCo asserts that claims

[1] The term "Pantoprazole" is used in this opinion to refer to both the compound itself and its sodium salt.
[2] For purposes of this Opinion Plaintiff Nycomed GmbH and Plaintiff Wyeth will be referred to collectively as "Plaintiffs."

22 and 25 of the '579 patent are, in fact, invalid for (1) obviousness under 35 U.S.C. § 103 in view of Compound 12 of the '518 patent; (2) double patenting in light of Compound 12 of the '518 patent; and (3) double patenting in light of Compound 4 of '230 patent. These issues as to KUDCo were tried non-jury from April 5-22, 2010.[3]

This Opinion constitutes the Court's findings of fact and conclusions of law pursuant to Fed. R. Civ. P. 52(a). For the reasons stated herein, a finding in favor of Plaintiff will be entered.

I. BACKGROUND[4]

A. THE '579 PATENT, "Pantoprazole"

Byk Gulden filed U.S. Patent Application 06/748,591 on June 14, 1985, which led to the issuance of the '579 patent. Final Pretrial Order ("Order") at 8, ¶ 1. The '579 patent claims priority to Swiss Application Nos. 2899/84 and 2901/84, both of which were filed on June 16, 1984. Order at 8, ¶ 3. Three inventors are named on the '579 patent: Bernard Kohl, Ernst Sturm, and Georg Rainer (the "Inventors"), all of whom were Byk Gulden employees in 1984. DX 1 at 1; Tr. (Kohl) at 5.82:1-4; 5.116:1-4; 5.119:15-21.[5] The '579 patent had already been assigned to Byk Gulden at the time it issued. DX 1 at 1. Nycomed, formerly Altana, presently owns the '579 patent. Order at 9, ¶ 6. The '579 patent expires on July 19, 2010. Order at 8, ¶ 4. The FDA awarded Wyeth a period of pediatric exclusivity that expires on January 19, 2011. Order at 9, ¶ 5.

The '579 patent makes various statements about the favorable properties of the disclosed compounds. Specifically, the '579 patent states that the "dialkoxypyridines of formula I and

[3] While KUDCo's invalidity defense and counterclaims were tried to this Court, a jury was empanelled to address issues as to the defenses and counterclaims of Teva and Sun. The jury's findings were advisory only and are in no way binding on this Court's consideration as to KUDCo. (See D.I. 535; D.I. 604.)

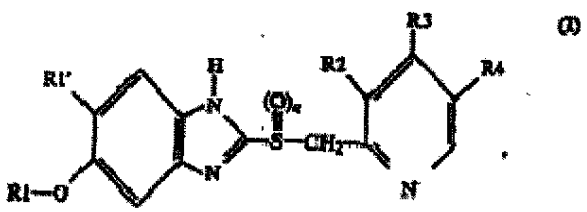
[4] The following facts are not in dispute unless otherwise noted.

[5] Throughout this opinion "DX" refers to Defendant's exhibits, "PX" refers to Plaintiffs' exhibits, and "Tr." refers to transcript.

their pharmacologically-acceptable salts have useful pharmacological properties which render them commercially useful." DX 1, col. 30, ll. 40-43; Tr. (Hopfinger) 10.129:15-21. The '579 patent asserts that the compounds "inhibit gastric acid secretion in warm-blooded animals" and "exhibit an excellent protective action on the stomach and intestines." DX 1, col. 30, ll. 43-46; Tr. (Sherman) 4.109:2-15; Tr. (Hopfinger) 10.130:4-15. The '579 patent states that the compounds "are distinguished by the absence of substantial side effects and by a wide therapeutic range." DX 1, col. 30, ll. 49-51; Tr. (Hopfinger) 10.131:11-132:1. The '579 patent also states that another advantage of the compounds disclosed in the patent "is their comparatively high chemical stability." DX 1, col. 30, ll. 63-65; Tr. (Sherman) 4.109:16-18; Tr. (Hopfinger) 10.164:22-165:6. The '579 patent further states that the compounds disclosed in the patent "are clearly superior (in their excellent properties) to prior art compounds." DX 1, col. 30, ll. 66-68; Tr. (Sherman) 4.109:19-21; Tr. (Hopfinger) 10.164: 2-21. Finally, the '579 patent states that the compounds disclosed in the patent "are outstandingly suitable for use in human and veterinary medicine." DX 1, col. 31, ll. 1-3; Tr. (Hopfinger) 10.132:25-133:13.

Claim 1 of the '579 patent, from which Claims 22 and 25 depend, reads as follows:

A dialkoxypyridine of formula I



(I)

Wherein R1 is 1-3C-alkyl which is completely or predominantly substituted by fluorine, or chlorodifluoromethyl; R1' is a hydrogen atom, halo, trifluoromethyl, 1-3-Calkyl, or 1-3C-alkoxy which is unsubstituted or completely or predominatly [sic] substituted by fluorine; or R1 and R1', together with the oxygen atom to which R1 is bonded, is l-2C-alkylenedioxy which is optionally completely or partly substituted by fluorine, or chlorotrifluoroethylenedioxy; R3 is l-3C-alkoxy; one of R2 and R4 is 1-3C-alkoxy and the other is a hydrogen atom or l-3C-alkyl;

and
n is 0 or 1;
or a salt thereof.

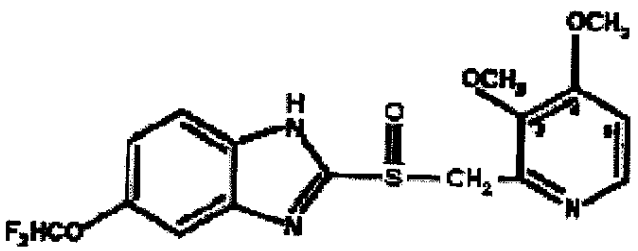
DX 1 at col. 33, ll. 25-50.

Claim 22 of the '579 patent reads as follows: "A compound according to claim 1 which is 5- difluoromethoxy-2-[(3,4-dimethoxy-2-pyridyl)methyl-sulfinyl]-1H-benzimidazole or pharmacologically compatible salt thereof." DX 1 at col. 35, ll. 10-14.

Claim 25 of the '579 patent reads as follows: "The compound according to claim 1 which is 5- difluoromethoxy-2-[(3,4-dimethoxy-2-pyridyl)methyl-sulfinyl]-1H-benzimidazole sodium salt." DX 1 at col. 36, ll. 4-7.

Claim 22 of the '579 patent covers the compound Pantoprazole and its pharmacologically compatible salts, and Claim 25 covers Pantoprazole sodium salt. (Tr. (Sherman) 4.43:1-44:11.)

The chemical structure of Pantoprazole is:

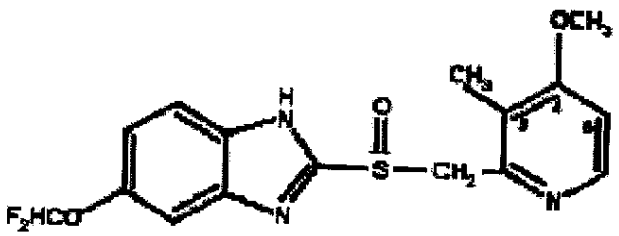


Tr. (Hopfinger) 9.97:21-9.98:2.

B. THE '518 PATENT

On May 1, 1984, Byk Gulden filed U.S. Application No. 606,872. This application eventually issued as the '518 patent on November 26, 1985. The '518 patent is entitled, "Fluoroalkoxy Substituted Benzimidazoles Useful as Gastric Acid Secretion Inhibitors." Order at 9, ¶¶ 10-11; DX 7 at 1. Georg Rainer is the named inventor on the '518 patent, and he was an employee of Byk Gulden in 1984. DX 7 at 1; Tr. (Kohl) 5.119:15-24. The '518 patent was

assigned to Byk Gulden at the time it issued. Order at 9, ¶ 12; DX 7 at 1. Compound 12 of the '518 patent is 5-difluoromethoxy-2-[(4-methoxy-3-methyl-2-pyridyl)-methylsylfinyl] 1Hbenzimidazole. DX 7, col. 24, ll. 46-47. The chemical structure of Compound 12 corresponding to the chemical name provided in the '518 patent is:



Tr. (Sherman) 4.85:20-23 (testimony regarding formal chemical name of Compound 12); Tr. (Sherman) 4.86:23-4.87:14 (testimony explaining the structure of Compound 12 using a demonstrative exhibit).

Compound 12 is also identified by name in Claim 16 of the '518 patent. (DX 7, col. 28, ll. 17-18; Tr. (Sherman) 4.85:5-23.) Claim 16 also covers "pharmacologically-acceptable salt[s]" of Compound 12. Tr. (Sherman) 4.85:24-86:23.

C. THE '230 PATENT

On October 29, 1985, Altana filed U.S. Application No. 794,230, which eventually issued as U.S. Patent No. 4,686,230 (the "230 patent"). Order at 8, ¶ 7. The '230 patent issued on August 11, 1987. Id. at ¶ 8. The '230 patent was assigned to Altana at the time it issued. Id. at ¶ 9. The '230 patent expired on August 11, 1999. Tr. at 11.176:24-177:10.

Compound 4 of Claim 12 of the '230 Patent ("Compound 4") (and its pharmacologically acceptable salt) has a 3,4 dimethoxy pyridine ring and a 5-difluoromethoxy, 4,6 dimethyl substituted benzimidazole ring. (DX11, col. 46:12-37; (Hopfinger) 11.61:18-11.62:24.)

Compound 4 is claimed as "5-difluoromethoxy-2[(3,4-dimethoxy-2-pyridyl)methyl-

sulphinyl]-4,6-dimethyl-1H-benzimidazole ... or a pharmacologically acceptable salt [of Compound 4]." DX11, col. 46:21-22 and 36-37.

D. INFRINGEMENT

Plaintiffs have asserted that Defendants have infringed and are infringing claims 22 and 25 of the 579 patent. Order at 10, ¶ 1. The Parties have reached a stipulation regarding the issue of infringement. Id. at ¶ 2; D.I. 617-619. More specifically, KUDCo has stipulated that its submission of ANDA No. 78-821 infringes claims 22 and 25 of the 579 patent if those claims are valid and enforceable and that KUDCo's making, using, offering for sale, selling in the United States, or importing into the United States of generic Pantoprazole sodium tablets under that ANDA would infringe claims 22 and 25 of the 579 patent if those claims are valid and enforceable. D.I. 618 at ¶ 1.

E. PERSON OF ORDINARY SKILL IN THE ART

The parties have stipulated to the definition of an ordinary skill in the art. Specifically, person of ordinary skill in the art is defined by stipulation as follows:

> ... a person of skill is someone having a graduate degree in one of the fields of medicinal chemistry, pharmacology, organic chemistry, biochemistry, or pharmaceutical chemistry, and practical experience in an academic or industrial laboratory. Such a person would also have collaborated extensively with those in the referenced fields other than her own, thus becoming knowledgeable in those fields, and also would have learned about patent prosecution of pharmaceuticals.

Order at 9, ¶ 2; (Sherman) 4.39:25-4.40:13; (Press) 6.86:1-4; (Hopfinger) 9.61:2-7. Additionally, both parties' experts testified that a person of ordinary skill in the art would have understood the core structure of a PPI embodied a benzimidazole ring and pyridine ring connected by a methylsulfinyl bridge. Tr. (Sherman) 4.67:11-21; Tr. (Carlsson) 8.164: 24-8.165:5. Medicinal chemists in 1984 knew the core, unsubstituted pyridine and benzimidazole

ring connected by a methylsufinyl bridge conferred the PPI activity to the class of molecules claimed in the '230 and '579 Patents. Tr. (Senn Bilfinger) 8.103:22 – 8.104:9; Tr. (Hopfinger) 11.64:21-23.

F. PRIOR ART

The parties agree that the prior art for purposes of evaluating the validity of the Asserted Claims of the 579 patent includes the following items received in evidence during trial:

a. Patents

i. U.S. Patent No. 4,045,563 ("the 563 patent") (DX 725)
ii. the 431 patent (DX 15)
iii. U.S. Patent No. 4,359,465 ("the 465 patent") (DX 772)
iv. U.S. Patent No. 4,472,409 ("the 409 patent") (DX 185)
v. U.S. Patent No. 4,508,905 ("the 905 patent") (DX 726)
vi. the 518 patent (DX 7)
vii. U.S. Patent No. 4,560,693 ("the 693 patent") (DX 641)
viii. U.S. Patent No. 5,077,407 (PX 156)
ix. U.S. Patent No. 4,575,554 (PX 187)
x. EP 0 074 341 (DX 638)

b. Other Publications

i. Bryson, A., "The Ionization Constants of 3-Substituted Pyridines, 3-Substituted Quinolines and 4-Substituted Isoquinolines," 82(18) J. Am. Chem. Soc'y 4871- 4877 (1960) ("Bryson") (DX 637)
ii. Larsson, et al., "Inhibition of Gastric Acid Secretion by Omeprazole in the Dog and Rat," 85 Gastroenterol. 900-907 (1983) ("Larsson") (DX 773)
iii. Perrin, D., "Dissociation Constants of Organic Bases in Aqueous Solution," International Union of Pure and Applied Chemistry (1965) ("Perrin") (DX 756)
iv. Sachs, G., "Pump Blockers and Ulcer Disease," New Engl. J. Med., 310 (12), 785-786 (1984) ("Sachs") (DX 980)
v. Sewing, et al., "Effect of Substituted Benzimidazoles on Acid Secretion in

Isolated and 10 Enriched Guinea Pig Parietal Cells," 24 Gut 557-560 (1983) ("Sewing") (DX 1154)

vi. Topliss, J., "Utilization of Operational Schemes for Analog Synthesis in Drug Design," 15(10) J. Med. Chem. 1006-1011 (1972) ("Topliss") (DX 646)

vii. Wallmark, et al., "Differentiation Among Inhibitory Actions of Omeprazole, Cimetidine, and SCN on Gastric Acid Secretion," 8(1) Am. J. Physiol., G64-G71 (1983) ("Wallmark I") (DX 640)

viii. Wallmark, et al., "Inhibition of Gastric (H+K)-ATPase by the Substituted Benzimidazole Picoprazole," 728 Biochemica et. Biophysica Acta 31-38 (1983) ("Wallmark II") (DX 774)

G. OVERVIEW OF TRIAL

A non-jury trial was conducted from April 5-22, 2010 with respect to KUDCo's affirmative defenses and counterclaims that Claims 22 and 25 of the '579 patent are invalid for obviousness and obviousness-type double patenting.[6] The Court heard testimony from ten witnesses, including seven expert witnesses. Defendants offered testimony from their experts, Dr. David Sherman, Dr. Duan Chen, Dr. Jeffery Press, and Dr. James Forstner. Defendants also called a named inventor on the '579 patent, Bernard Kohl, as an adverse witness during their case-in-chief. Plaintiffs offered testimony from their experts, Dr. Enar Carlsson, Dr. Richard Killworth, and Dr. Anton Hopfinger. Plaintiffs also offered testimony from a current employee, Geno Germano, and a former employee, George Senn-Bilfinger.

H. ADVISORY JURY'S FINDINGS[7]

a. With respect to the questions regarding Defendant's defense of invalidity based on Compound 12 the advisory jury found the following:

Have the defendants proven by clear and convincing evidence that a person of ordinary

[6] During this same time, a jury trial was conducted as to Defendant Teva and Defendant Sun. The jury's verdict with respect to Defendant Teva and Defendant Sun is the subject of motions filed pursuant to Fed. R. Civ. Pr. 50(b) currently pending before this Court.

[7] These findings are not binding on the Court pertaining to the analysis as to Defendant KUDCo.

skill in the art would have:

(1) had a reason or motivation to select Compound 12 as a starting point? (A "YES" answer is a finding for Teva, Sun and KUDCo. A "NO" answer is a finding for Nycomed and Wyeth.)

Yes____ No__X___

(2) had a reason or motivation to modify Compound 12 to arrive at pantoprazole? (A "YES" answer is a finding for Teva, Sun and KUDCo. A "NO" answer is a finding for Nycomed and Wyeth.)

Yes_____ No__X___

(3) have reasonably expected success? (A "YES" answer is a finding for Teva, Sun and KUDCo. A "NO" answer is a finding for Nycomed and Wyeth.)

Yes_____ No__X___

Secondary Considerations

(4) Which of the following factors, if any, has been established by the evidence with respect to the claimed invention – check any that apply:

__X__ commercial success of a product due to the merits of the claimed invention rather than due to advertising, promotion, salesmanship, or features of the product other than those known in the prior art or otherwise not attributable to the claimed invention

__X__ long felt need for a solution to the problem facing the inventors, which was satisfied by the claimed invention

__X__ others trying but failing to solve the problem solved by the claimed invention.

_____ copying of the claimed invention by others.

__X__ unexpected and superior results from the claimed invention over Compound 12 with regard to pH5 stability.

__X__ unexpected and superior results from the claimed invention over Compound 12 with regard to sodium-potassium pump selectivity.

_____ acceptance by others of the claimed invention as shown by the licensing of the claimed invention.

(5) If you answered yes to all of questions (1), (2) **and** (3), and considering your answers to question (4) above, do you find that Teva, Sun, and KUDCo have proven by clear and convincing evidence that claims 22 and 25 of the '579 patent would have been obvious in light of Compound 12 of the '518 patent to a person of ordinary skill in the art? (A "YES" answer is a finding for Teva, Sun and KUDCo. A "NO" answer is a finding for Nycomed and Wyeth.)
Yes_____ No __X___

(6) If you answered yes to all of questions (2) **and** (3), and considering your answers to question (4) above, do you find that Teva, Sun, and KUDCo have proven by clear and convincing evidence that claims 22 and 25 of the '579 patent are invalid based on double patenting? (A "YES" answer is a finding for Teva, Sun and KUDCo. A "NO" answer is a finding for Nycomed and Wyeth.)
Yes_____ No __X___

b. With respect to Defendant's defense of invalidity based on Compound 4 the jury found the following:

Have defendants proven by clear and convincing evidence that a person of ordinary skill in the art would have:

(7) had a reason or motivation to modify Compound 4 to arrive at pantoprazole? (A "YES" answer is a finding for Teva, Sun and KUDCo. A "NO" answer is a finding for Nycomed and Wyeth.)

Yes_____ No __X__

(8) reasonably expected success? (A "YES" answer is a finding for Teva, Sun and KUDCo. A "NO" answer is a finding for Nycomed and Wyeth.)

Yes_____ No __X__

Secondary Considerations:

(9) Which of the following factors, if any, has been established by the evidence with respect to the claimed invention – check any that apply:

_____ commercial success of a product due to the merits of the claimed invention rather than due to advertising, promotion, salesmanship, or features of the product other than those known in the prior art or otherwise not attributable to the claimed invention

_____ long felt need for a solution to the problem facing the inventors, which was satisfied by the claimed invention

_____ others trying but failing to solve the problem solved by the claimed invention.

_____ copying of the claimed invention by others.

_____ acceptance by others of the claimed invention as shown by the licensing of the claimed invention.

(10) If you answered yes to all of questions (7) **and** (8), and considering your answers to question (9) above, do you find that Teva, Sun, and KUDCo have proven by clear and convincing evidence that claims 22 and 25 of the '579 invalid based on double patenting?? (A "YES" answer is a finding for Teva, Sun and KUDCo. A "NO" answer is a finding for Nycomed and Wyeth.)
Yes_____ No__X___

II. APPLICABLE LAW

A patent issued by the Patent & Trademark Office is presumed valid. 35 U.S.C. § 282. The burden of establishing invalidity of a patent or any claim thereof rests on the party asserting invalidity. Id. A party seeking to prove a patent is invalid must do so by clear and convincing evidence. Takeda Chemical Indus. v. Alphapharma Pty. Ltd., 492 F.3d 1350, 1355 (Fed. Cir. 2007).

A. OBVIOUSNESS UNDER 35 U.S.C. § 103

Under 35 U.S.C. § 103(a),

> [a] patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious as the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

35 U.S.C. § 103(a). Obviousness depends on an objective analysis by the fact-finder of (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) any relevant secondary considerations. Graham v. John Deere Co., 383 U.S. 1, 18 (1966). As the Supreme Court noted, "[w]hile the

sequence of these questions might be reordered in any particular case, the factors continue to define the inquiry that controls. If a court, or patent examiner, conducts this analysis and concludes the claimed subject matter was obvious, the claim is invalid under § 103." KSR Int'l Co. v. Teleflex Inc., et al., 550 U.S. 398, 407 (2007).

To determine whether a patent is obvious, a Court "must step back in time to before the moment of actual invention, and out of the actual inventor's shoes into those of a hypothetical, ordinary skilled person who has never seen the invention." Eisai Co. v. Teva Pharms. USA, Inc., 2006 U.S. Dist. LEXIS 73516, at *5-6 (S.D.N.Y. Oct. 5, 2006) (citing W.L. Gore & Assocs., Inc. v. Garlock, Inc., 721 F.2d 1540, 1553 (Fed. Cir. 1983)). A finding of obviousness, then, "cannot be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention." Crown Operations Int'l, Ltd. v. Solutia, Inc., 289 F.3d 1367, 1376 (Fed. Cir. 2002)(quoting ATD Corp. v. Lydall, Inc., 159 F.3d 534, 546 (Fed. Cir. 1998).

B. NON-STATUATORY OBVIOUSNESS

The judicially-created doctrine of obviousness-type double patenting prohibit a party from obtaining an extension of the right to exclude through claims in a later patent that are not patentably distinct from claims in a commonly owned earlier patent. In re Longi, 759 F.2d 887, 892 (Fed. Cir. 1985). "The purpose of the rule against double patenting is to prevent an inventor from effectively extending the term of exclusivity by the subsequent patenting of variations that are not patentably distinct from the first-patented invention." Applied Materials Inc. v. Advanced Semiconductor Materials Am., Inc., 98 F.3d 1563, 1568 (Fed. Cir. 1996); Procter & Gamble Co. v. Teva Pharms. USA, Inc., 566 F.3d 989, 999 (Fed. Cir. 2009) ("The double patenting doctrine is designed to prevent a patent owner from extending his exclusive rights to an invention through

claims in a later-filed patent that are not patentably distinct from claims in the earlier filed patent.").

Non-statutory double patenting entails a two-pronged analysis. "First, as a matter of law, a court construes the claim in the earlier patent and the claim in the later patent and determines the differences." Eli Lilly v. Barr Laboratories, Inc., 251 F.3d 955, 968 (Fed. Cir. 2001) (citing Georgia-Pacific Corp. v. United States Gypsum Co., 195 F.3d 1322, 1326 (Fed. Cir. 1999)). "Second, the court determines whether the differences in subject matter between the two claims render the claims patentably distinct." Id. (citing Georgia Pacific, 195 F.3d at 1327). If the later claim is an "obvious variant" or obvious modification of the earlier claim, then the later claim is invalid for non-statutory double patenting. In re Basell Poliolefine Italia S.P.A., 547 F.3d 1371, 1378-79 (Fed. Cir. 2008). With respect to step two, whether or not the claims are "patentably distinct" involves "ask[ing] whether the identified difference renders the claims of the ... [two] patents non-obvious to a person of ordinary skill in the art in light of the prior art." Amgen v. F. Hoffman-LA Roche, Ltd., 580 F.3d 1340, 1361 (Fed. Cir. 2009); see also Pfizer, Inc. v. Teva Pharms. USA, Inc., 518 F.3d 1353, 1363 (Fed. Cir. 2008); In re Kaplan, 789 F.2d 1574, 1580 (Fed. Cir. 1986). "This part of the obviousness-type double patenting analysis is analogous to an obviousness analysis under 35 U.S.C. § 103, except that the [alleged invalidating reference] is not considered prior art." Amgen, 580 F.3d at 1361. Specifically, obviousness-type double patenting analysis requires an inquiry into the scope and content of the prior art, the level of skill in the art, and what would have been obvious to a person skilled in the art. See Studiengesellschaft Kohle mbH v. N. Petrochemical Co., 784 F.2d 351, 355 (Fed. Cir. 1986).

III. DISCUSSION

A. OBVIOUSNESS UNDER 35 U.S.C. § 103

Defendant KUDCo argues that it has established a *prima facie* case of obviousness by simply demonstrating the structural similarity between Compound 12 of the '518 patent and Pantoprazole. This position, however, is at odds with Federal Circuit precedent, including its decision to uphold this Court's denial of Plaintiff's motion for a preliminary injunction where it held that "[o]bviousness based on structural similarity may be proven by the identification of some motivation that would have led one of ordinary skill in the art to select and modify a known compound in a particular way to achieve the claimed compound." Altana Pharma AG v. Teva Pharmas. USA, Inc., 566 F.3d 999, 1007 (Fed. Cir. 2009) (see also Takeda Chemical Industries, Ltd. v. Alphapharm Pty. Ltd., 492 F.3d 1350, 1356 (Fed. Cir. 2007) ("We have held that structural similarity between claimed and prior art subject matter, proved by combining references or otherwise, where the prior art gives reason or motivation to make the claimed compositions, creates a *prima facie* case of obviousness. . . . [I]n order to find a *prima facie* case of unpatentability in such instances, a showing that the prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention was also required.")(internal quotations and citations omitted); Yamanouchi Pharm. Co. v. Danbury Pharma., Inc., 231 F.3d 1339, 1343 (Fed. Cir. 2000) quoting In re Dillion, 919 F.2d 688, 692 (Fed. Cir. 1990) (en banc) ("For a chemical compound, a *prima facie* case of obviousness requires 'structural similarity between claimed and prior art subject matter . . . where the prior art gives reason or motivation to make the claimed compositions.'") Thus, structural similarity alone is insufficient to prove a *prima facie* case of obviousness. Therefore, this Court finds that the burden has not yet shifted to the Plaintiffs. This Court, as the fact finder, therefore proceeds to

conduct an analysis of (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) any relevant secondary considerations. Graham, 383 U.S. at 18. Inasmuch as the parties stipulated to the scope, content, and level of ordinary skill in the art, the Court proceeds directly to the third and fourth prongs of the analysis.

a. The differences between the claimed invention and the prior art.

When patents on chemical compounds are at issue, the following factual considerations have been analyzed in the context of evaluating the differences between the claimed invention and the prior art: (a) whether there would have been a reason or motivation to select a known prior art compound as a starting point; (b) whether there would have been a motivation to modify that known compound in a particular way to achieve the claimed compound; and (c) whether there would have been a reasonable expectation of success in making that modification. See, e.g., Procter & Gamble Co., 566 F.3d at 994.; Eisai Co. v. Dr. Reddy's Labs., Ltd., 533 F.3d 1353, 1359 (Fed. Cir. 2008); Takeda, 492 F.3d at 1360; Yamanouchi, 231 F.3d at 1344-45 (Fed. Cir. 2000). The Court will now analyze each factual consideration in turn.

i. Reason or motivation to select a known prior art compound as a starting point.

Defendant argues, based on Dr. Sherman's testing, that one of ordinary skill in the art would have been motivated to select Compound 12 as a starting point because "if one considers the structure of that molecule and makes the obvious insertion of an oxygen atom, a single oxygen atom at C3 on the pyridine ring, that molecule is pantoprazole." Tr. (Sherman) at 5.20:23-24:17. However, Dr. Sherman also testified that he was aware of Pantoprazole's chemical structure prior to conducting his lead compound analysis. This fact makes Dr. Sherman's testimony regarding his selection of Compound 12 as the lead compound

unpersuasive. Unlike a person skilled in the art in 1984, Dr. Sherman was afforded the benefit of knowing the desired end result of the chemical structure prior to choosing Compound 12 as a lead compound and, thus, has the impermissible benefit of hindsight. ATD Corp. v. Lydall, Inc., 159 F.3d 534, 546 (Fed. Cir. 1998) ("Determination of obviousness cannot be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention."). This knowledge taints Dr. Sherman's lead compound analysis and, therefore, cannot be considered to be clear and convincing evidence that a person of ordinary skill in the art in 1984 would have had reason or motivation to select Compound 12 of the '518 patent as a starting point.

In contrast, Plaintiff provided ample evidence which indicates that Omeprazole would have been the most logical starting point in 1984. As of 1984, Omeprazole was the only PPI that had been tested in humans. Tr. (Carlsson) at 8.141:3-7. Logically, this fact would make a person skilled in the art look to this drug as a starting point since it had already been deployed for that particular use in humans.

ii. Motivation to modify that known compound in a particular way to achieve the claimed compound.

Defendant argues that the one skilled in the art would have been motivated to modify Compound 12 into Pantoprazole because (1) "the Sachs Article" gave one of ordinary skill in the art a reason to seek out a PPI with beneficial characteristics similar to those of Compound 12, but with a pKa of 4, and (2) the Bryson and Perrin references independently establish that one of ordinary skill in the art in 1984 had a reason to substitute a methoxy at the 3-position of the pyridine ring of Compound 12. For the following reasons, the Court finds that Defendant failed to demonstrate by clear and convincing evidence that a person of ordinary skill in the art would have had motivation to modify Compound 12 of the '518 patent as a way to achieve

Pantoprazole.

First, the Court finds that the Sachs Article (DX 980) would not have provided a person of skill in the art with a reason or motivation to modify Compound 12 to arrive at Pantoprazole. Although the Sachs Article discussed two desirable qualities with respect to PPI's – namely, Activation and Accumulation – it does not teach how to achieve either quality. Tr. (Hopfinger) at 9.131:25-132:6. Moreover, the Sachs Article specifically references Omeprazole as having a desirable quality. Therefore, although a person skilled in the art would be aware of a theoretical desired characteristic based on the Sachs Article, said article did not provide that person with a particular way to modify Compound 12 to achieve that preferred quality. Additionally, the Court notes that the Sachs Article would encourage a person of skill in the art to focus on Omeprazole as a lead compound as it demonstrated a desired quality for a PPI.

Second, the Defendant argues that the Bryson and Perrin references independently establish that one of ordinary skill in 1984 had a reason to substitute a methoxy at the 3-position of the pyridine ring of Compound 12. The Court finds the Bryson and Perrin references unpersuasive. Dr. Sherman, an expert called to testify on behalf of the Defendant, stated that it is inappropriate to compare compounds of different classes with respect to structure-activity relationships as the results would be unpredictable. Tr. (Sherman) at 4.155:3-10; 4.208:19-209:1. The Bryson and Perrin references concern only one piece of the PPI backbone – the pyridine ring – and did not consider the relationship of the pyridine ring to the PPI backbone as a whole. In other words, according to the Defendant's expert, a comparison of an isolated pyridine ring to a PPI is inappropriate as each belongs to a different class of compounds. Bryson's and Perrin's teachings concerning the pKa of isolated pyridines could not, therefore, have been used by a person of ordinary skill in the art in June 1984 to predict the effect of a substituent change on the

pyridine ring of a PPI molecule because the remainder of the PPI molecule can significantly alter that behavior and the properties of the pyridine ring. Tr. (Hopfinger) at 9.154:24-155:3. Therefore, the Court finds Defendant's reliance on the teachings of Bryson and Perrin unpersuasive.

For the foregoing reasons, the Court finds that Defendant failed to show by clear and convincing evidence a motivation to modify Compound 12 in a particular way to achieve Pantoprazole.

iii. Reasonable expectation of success in making that modification.

The Court finds that that one of ordinary skill in the art would not have reasonably expected that the substitution of a methoxy instead of a methyl at the 3-position of Compound 12's pyridine ring would succeed in producing a compound that retained beneficial properties similar to those of Compound 12 but that had a pKa of 4. The Court is persuaded by Dr. Hopfinger's testimony that one of ordinary skill in the art in 1984 would have been unable to make such a prediction and finds that Defendant failed to provide clear and convincing evidence to the contrary. See, e.g., Tr. (Hopfinger) 9.142:3-10 ("[T]here simply is no reliable way of – of – of predicting pKa. There's no reliable structure activity relationship. You are kind of hopelessly lost at sea."); 9.164:14-15 ("PPIs were basically unpredictable and remain unpredictable.") Defendant contends that the Brandstrom article concerning PPI's directly contradicts Dr. Hopfinger's testimony by teaching that "[t]he [changes in pKa] values are usually additive, which means that the . . . value for a poly-substituted pyridine is the sum . . . of the individual . . . values of each substituent." DX 1013 at 18. The Court finds said contention unpersuasive as its date of publication falls outside the relevant time period of prior art and, moreover, is not one of the stipulated prior art references.

b. Objective Indicia of Non-Obviousness (Secondary Considerations)

The final factor of the obviousness analysis requires the fact finder to assess whether the following objective indicia of non-obviousness sufficiently rebut a *prima facie* case of obviousness. See, e.g., Eli Lilly & Co. v. Zenith Goldline Pharms., Inc., 471 F.3d 1369, 1380 (Fed. Cir. 2006). Here, the Court finds that even if Defendant had established a *prima facie* case of obviousness, which the Court finds that it has not, the evidence of record in support of the relevant objective indicia of non-obviousness would sufficiently rebut said *prima facie* case. Inasmuch as Defendant failed to establish a *prima facie* case of obviousness, the Plaintiffs did not have the burden to present evidence of non-obviousness. Even so, in the interests of completeness, the Court will discuss said evidence.[8]

i. Commercial Success

In support of commercial success, Plaintiffs attempted to introduce the opinion of Geno Germano, a Wyeth marketing executive. The Court, however, sustained Defense Counsel's objection that Mr. Germano was unqualified to give an opinion as to whether the success of pantoprazole came from its active ingredient, and struck (and therefore will not consider in this decision) his testimony regarding said opinion. Thereafter, Plaintiffs offered no other credible evidence of commercial success. However, as previously stated, because Defendant failed to make a prima facie case of obviousness the burden did not shift to Plaintiffs to present objective indicia of non-obviousness as to this issue of non-obviousness or any other objective indicia of non-obviousness. Nevertheless, the Court finds no indicia of commercial success.

ii. Long-Felt Need

Plaintiffs contend that Pantoprazole satisfied a long-felt need because it provided a

[8] To the extent that the Court's findings of fact conflict with the jury's findings of fact with respect to secondary considerations, said conflict is immaterial since the jury's findings as to KUDCo were merely advisory and in no way binding.

superior alternative to Omeprazole during a time when Omeprazole – the first PPI – was thought to cause tumors in rats. Tr. (Carlsson) at 8.142:3-11. More specifically, Plaintiffs produced evidence they argue indicates that due to the worldwide suspension of clinical trials of Omeprazole between May 1984 and sometime in 1986, there was a need to find a PPI that would be suitable for human use. Plaintiffs argue that Pantoprazole filled that long-felt need.

The Court finds that Plaintiffs, however, failed to demonstrate that any long-felt but unsolved need was met by a "claimed and novel feature[]" of Pantoprazole. Ormco Corp. v. Align Tech.,Inc., 463 F.3d 1299, 1313 (Fed. Cir. 2006). Although Plaintiffs argue that in 1984 Omeprazole had not yet met a need for a PPI that would be suitable for use in humans due to fears that it caused tumors in rats, Plaintiffs failed to identify a feature of pantoprazole that was relevant to this alleged need. Furthermore, Omeprazole was later shown not to produce tumors. Accordingly, the Court finds that Plaintiffs offered no credible evidence of long-felt need. However, the Court again notes that Defendant failed to make a prima facie case of obviousness and, therefore, as was the case with commercial success, Plaintiff did not have the burden to present any objective indicia of non-obviousness as to long-felt need.

iii. Failure of Others

In support of failure of others, Plaintiffs state that many scientists failed in their attempts to find an approvable PPI that would be an improvement over Omeprazole. The scientists at Searle failed. Tr. (Hopfinger) at 9.163:15-164:2. Specifically, fifteen to twenty scientists over a seven year period failed to discover a PPI that made it to the marketplace. (Id.) Dr. Press and the other medicinal chemists at Ortho likewise failed to discover a compound that was better than Omeprazole. Id. (Press) at 6.133:8-134:7. The four labs of medicinal chemists at Altana synthesized about 600 compounds over a four to five year period. Id. (Senn-Bilfinger) at

8.52:17-53:4. None of those compounds ever made it to the market. Id. (Senn-Bilfinger) at 8.46:1-23.

Here, had the burden to prove objective indicia of non-obviousness shifted, the Plaintiffs would have been required to show that "prior attempts failed because the devices lacked the claimed features." Ormco, 463 F.3d at 1313. Plaintiffs offered no evidence that the factor that differentiated pantoprazole from the prior art – the use of a methoxy group instead of a methyl group at the 3-position of the pyridine ring of Compound 12 – was the reason they succeeded while others allegedly failed. Accordingly, the Court finds that Plaintiffs offered no evidence of failure of others.

iv. Unexpected Superior Results / pH5 Stability

In support of unexpected superior results, Plaintiffs point to Pantoprazole's pH5 Stability. A compound is considered stable at pH 5 when the compound will not activate in a pH 5 environment. Tr. (Hopfinger) at 9.124:10-14. The parties agree that in the 1980s, the pH 5 stability of PPI compounds was a major concern in the field. Id. (Sherman) at 5.66:19-67:2 (Sherman); Id. (Senn-Bilfinger) at 8.33:9-17; Id. (Hopfinger) at 9.126:5-7. Specifically, both parties presented testimony that pH 5 stability was viewed as an important feature of PPI compounds in June of 1984 because there was a concern about side effects if the PPIs could activate in areas of the body other than the parietal cells. Id. (Senn-Bilfinger) at 8.36:6-9; Id. (Hopfinger) at 9.125:14-126:23; Id. (Sherman) at 5.66:19-67:21; Id. (Carlson) at 8.167:9-169:4.

Plaintiffs presented evidence that Pantoprazole had superior pH5 stability as compared to Compound 12 of the 518 patent through Dr. Hopfinger's explanation of Dr. Krug's, an Altana scientists, declaration. Specifically, Dr. Hopfinger explained that Compound 12 is shown to have a pH 5 stability or half-life of 0.8 hours, whereas pantoprazole has a half-life of 21 hours.

Tr. (Hopfinger) at 9.176:3-8; PX 2 at AP322967.) In other words, in a pH 5 environment, pantoprazole will maintain itself and its integrity for a longer period of time than Compound 12. Id. (Hopfinger) at 9.176:11-15.

Plaintiffs also presented evidence showing that Pantoprazole showed greater pH5 stability than Compound 12 in a solvent system different from that which was used for the tests reported in the Kruger declaration. DX 849 at 1053; Tr. (Hopfinger) at 9.176:16-177:1. The 1992 Journal of Medicinal Chemistry article reported that the pH5 stability half-life of pantoprazole is three hours and that the pH 5 stability half-life of Compound 12 is 0.17 hours. DX 849 at 1053; Tr. (Hopfinger) at 9.177:7-13. Here, again, this supports the conclusions that pantoprazole will maintain itself and its integrity for a longer period of time than Compound 12. The Court finds that the credible and persuasive evidence presented regarding Pantoprazole's superior pH5 stability would have met Plaintiffs' burden had Defendants proved a *prima facie* case of obviousness.

Plaintiffs also demonstrated that this superior quality was, in fact, unexpected in June 1984 because (1) in June 1984, a person of ordinary skill in the art would not have been able to predict that pantoprazole would have superior pH 5 stability compared to Compound 12 (Tr. Hopfinger) at 9.177:14-24) and (2) the 518 patent makes no mention of pH 5 stability with respect to Compound 12 or any other compound. DX 7; Tr. (Sherman) at 5.66:15-18; Id. (Hopfinger) at 10.29:20-30:3. As such, the Court finds that Plaintiffs presented evidence in support of unexpected superior results related to Pantoprazole's pH5 stability despite the fact that they were not required to in light of Defendant's failure to prove a prima facie case.

v. Unexpected Superior Results / Sodium-Potassium Pump Selectivity

In support of unexpected superior results, Plaintiffs introduced evidence that in June

1984, in comparison to Compound 12, pantoprazole had superior selectivity for the proton pump as opposed to the sodium-potassium pump. There are other pumps within the body other than the proton pump. Tr. (Sherman) at 4.153:10-12; Id. (Hopfinger) at 9.167:17-25. One of those is the sodium-potassium pump. Id. (Hopfinger) at 9.167:17-25. Sodium-potassium pumps are found throughout the body and are particularly important to cardiac tissue and cardiac function. Id. (Hopfinger) at 9.168:1-6. Because the proton pump and the sodium-potassium pump are similar, there was a concern that shutting down the proton pump might interfere with the sodium-potassium pump. Id. (Hopfinger) at 9.168:7-20. Scientists wanted to avoid shutting down the sodium pump to avoid side effects or cardio toxicity. Id. (Hopfinger); Id. (Sherman) at 4.153:13-20. In June 1984, one of skill in the art wanted to be sure that a PPI compound was turning off the proton pump, but not turning off other pumps. Id. (Sherman) at 4.153:13-20. This can be defined as *selectivity* and is a desirable feature for PPI compound. Id. (Hopfinger) at 9.168:21-169:7.

Dr. Hopfinger's testimony amply supports Plaintiffs' contention that Pantoprazole had superior selectivity for the proton pump as opposed to the sodium-potassium pump. For instance, Dr. Hopfinger explained, by reference to the Journal of Medicinal Chemistry, that Pantoprazole has 40 times greater selectivity for the proton pump than the sodium-potassium pump. Tr. (Hopfinger) at 9.172:6-15; DX 849 at 1053.) Dr. Hopfinger went on to explain that this means that pantoprazole shuts down the proton pump 40 times more than the sodium-potassium pump. Tr. (Hopfinger) at 9.172:6-15. In contrast, Compound 12 has only around 11 times greater selectivity for the proton pump than the sodium-potassium pump. (Id.; DX 849 at 1053.) Dr. Hopfinger explained that Pantoprazole's greater selectivity is significant to a medicinal chemist because it means that pantoprazole will have much less interference with the

sodium-potassium pump as compared to Compound 12. Id. (Hopfinger) at 9.173:2-8.

Defendant was unable to discredit Dr. Hopfinger's testimony on cross-examination. Defendants used two publications during Dr. Hopfinger's cross-examination in an effort to suggest that Pantoprazole's improved selectivity over Compound 12 would have been expected in 1984. (DX 774; DX 822.) Neither article, however, supports that view.

Wallmark II (DX 774), which was published in 1983, discussed some experiments concerning whether a single PPI compound – picoprazole – inhibited the sodium-potassium pump. DX 774; Tr. (Hopfinger) at 11.39:5-40:9. Although the article does show that there were concerns regarding the possible interaction of PPIs with the sodium-potassium pump as early as 1983, this article did not address any other PPI compound besides picoprazole. ((DX 822; DX 849; Tr. (Hopfinger) at 11.168:12-169:6. Therefore, it proved little or nothing about what would have been expected with respect to pantoprazole, Compound 12, or any other PPI (except picoprazole) as of June 1984.

The second article, published in 1987 titled "Specificity of the Substituted Benzimidazole B823-08: A Prodrug for Gastric Proton Pump Inhibition" discussed some experiments conducted to determine if two specific PPI compounds would affect the sodium-potassium pump. (DX 822; Tr. (Hopfinger) at 11.50:6-10; (Hopfinger)11.165:18-23. The Court finds the teachings of this article unpersuasive with respect to Compound 12 and pantoprazole because said article does not reference either compound, and thus, offers nothing to suggest how Pantoprazole itself would affect the sodium-potassium pump.

The Court hereby finds that Plaintiffs presented evidence in support of unexpected superior results related to Pantoprazole's superior selectivity for the sodium-potassium pump despite not having to do so.

vi. Copying of the claimed invention by others.

"[A] showing of copying is only equivocal evidence of non-obviousness in the absence of more compelling objective indicia of other secondary considerations." Ecolochem, Inc. v. S. Cal. Edison Co., 227 F.3d 1361, 1379 (Fed. Cir. 2000); see also In re GPAC, 57 F.3d 1573, 1580 (Fed.Cir.1995) ("'[M]ore than the mere fact of copying by an accused infringer is needed to make that action significant to a determination of the obviousness issue.'") (quoting Cable Elec. Prods. v. Genmark, Inc., 770 F.2d 1015, 1028 (Fed. Cir. 1985)). Plaintiffs claim that Defendant copied the claimed invention – pantoprazole sodium – by submitting regulatory filings seeking to commercialize generic versions of that compound. Defendant did not provide evidence or argument to the contrary. Defendant, when filing its ANDA, was obligated to apply for the same exact invention. See 21 U.S.C.A. Section 355(j)(2)(A)(ii)(I). Thus, by law, Defendant copied Pantoprazole. Accordingly, the Court finds that the presented evidence supports a finding of copying – but notes that it affords little, if any, weight in favor of non-obviousness. As such, the Court finds that despite the fact that Plaintiffs presented evidence in support of copying, even though they were not required to do so in light of Defendant's failure to prove a prima facie case, such evidence in and of itself is not evidence of non-obviousness.

vii. Acceptance by others of the claimed invention as shown by the licensing of the claimed invention.

Another secondary consideration is the "acceptance by others of the claimed invention as shown . . . from licensing of the claimed invention." Ecolochem, 227 F.3d at 1376-81. Plaintiffs argue that this license agreement and its specific terms is evidence of acceptance by others of the compound covered by the Asserted Claims. Wyeth has an exclusive license to the 579 patent in the United States. PX 22; Tr. (Germano) at 7.194:2-199:19. The preamble to the License Agreement between Wyeth and Altana states:

> [Wyeth] is interested in cooperating with [Altana] in the development, marketing and sales of Pantoprazole in the United States on a long-term basis, and is therefore not only interested in a license to the Product and the Compound during Patent protection, but also interested in assuring itself of a long-term source of supply of the Compound before and after Patent expiry and is thus prepared to enter into a license agreement, as well as into a longterm supply agreement.

PX 22 at 321004 ¶ 6; Tr. (Germano) at 7.198:2-13. Defendant did not provide evidence or argument to the contrary. Accordingly, the Court finds that Plaintiff presented evidence in support of acceptance by others despite the fact that they were not required to in light of Defendant's failure to prove a *prima facie* case.

B. NON-STATUATORY OBVIOUSNESS

Non-statutory double patenting entails a two-pronged analysis. "First, as a matter of law, a court construes the claim in the earlier patent and the claim in the later patent and determines the differences." Eli Lilly, 251 F.3d at 968 (citing Georgia-Pacific, 195 F.3d at 1326. "Second, the court determines whether the differences in subject matter between the two claims render the claims patentably distinct." Id. (citing Georgia Pacific, 195 F.3d at 1327). Here, there is no dispute regarding step one (claim construction) because the claims at issue involve specific chemical compounds – Compound 12, Compound 4, and pantoprazole. Therefore, the Court's analysis is confined to the second prong, namely "whether the differences in subject matter between the two claims render the claims patentably distinct." Id. (citing Georgia Pacific, 195 F.3d at 1327).

a. Not Obvious in light of Compound 12 of the '518 Patent

Again, with respect to step one (claim construction) the Parties agree that the sole difference between Compound 12 (Claim 16 of the '518 patent) and pantoprazole (claims 22 and 25 of the '579 patent) is that Compound 12 has a methyl group at the 3-position of the pyridine

ring, while pantoprazole has a methoxy group at that position. Therefore, the only disputed issue is whether the pantoprazole and Compound 12 of the '518 are patentably distinct.

Because the obviousness-type double patenting analysis and the obviousness analysis under § 103 are parallel, the Court finds that the outcome of Defendant's two defenses based on Compound 12 must be the same. Therefore, as the Court has found that the record of evidence does not support Defendant's § 103 defense based on Compound 12, it likewise does not support of a defense of obviousness in light of Compound 12 of the '518 patent. See, e.g., Procter & Gamble, 566 F.3d at 999 ("Having concluded that risedronate was not obvious under 35 U.S.C. § 103, we similarly conclude that the '122 patent is not invalid for obviousness type double patenting."); Sanofi-Synthelabo v. Apotex, Inc., 488 F. Supp. 2d 317, 338 (S.D.N.Y. 2006), aff'd 470 F.3d 1368 (Fed. Cir. 2006) ("If Apotex fails to prove at trial that the '265 patent was obvious in light of the '596 patent as a whole, it has also necessarily failed to prove that the '265 patent was obvious in light of the specific claims of the '596 patent."). Accordingly, the Court shall enter judgment against Defendant on its double patenting defense based on Compound 12.

b. Not Obvious in Light of Compound 4 of the '230 Patent

Here again, with respect to step one, the Parties agree that the only difference between Compound 4 of the '230 patent and pantoprazole is that on the 4- and 6- positions of the benzimidazole rings, Compound 4 has methyl (-CH3) groups and pantoprazole has hydrogens (-H). Therefore, the only disputed issue is whether pantoprazole and Compound 4 of the '230 patent are patentably distinct.

The Defendant offered testimony from two witnesses regarding double patenting with respect to Compound 4 of the 230 patent. First, Dr. Chen testified about tests he performed comparing the inhibitory effect of Compound 4 and pantoprazole on acid secretion in rats. Then,

Dr. Press offered the opinion that pantoprazole represented an "obvious modification" of Compound 4. The Court will address each experts' testimony in turn.

i. Dr. Chen

Dr. Chen administered Compound 4 and pantoprazole to two different sets of rats and then measured acid secretion in the animals. (Id. at 6.18:4-19:7 (Chen).) Two different studies were performed, one lasting twenty-two hours and the other lasting an additional twenty-four hours. Id. (Chen) 6.19:15-18. Dr. Chen testified that the "[t]he scientific conclusion from [his] study is there is insufficient evidence to suggest the two compounds, namely pantoprazole and Compound 4, differ from each other with respect to their inhibition of acid secretion in rats." Id. at (Chen) 6.21:23-22:2. The Court finds Dr. Chen's testimony unpersuasive.

Dr. Chen's ultimate scientific conclusion that there is a lack of evidence to show that the compounds are different does not prove the opposite conclusion or indicate by clear and convincing evidence that Pantoprazole represents an obvious modification of Compound 4. Second, it does not appear that Dr. Chen performed his testing or formed his ultimate conclusions from the perspective of a person skilled in the art as of June 1984, but rather was armed with present day knowledge. Finally, Plaintiffs' expert, Dr. Carlsson, credibly challenged Dr. Chen's testing protocol regarding duration of action (how long a given chemical compound is effective). Id. (Carlsson) at 8.147:19-25. Specifically, Dr. Carlson testified that in order to perform a reliable test with rats, it is necessary to dose the rats at a level that allows acid secretion to resume as the drug wears off until acid levels have reached the levels of a control. Id. (Carlsson) at 8.150:1-9. Although Dr. Carlson agreed with Dr. Chen's protocol to starve the rats, Dr. Carlson went on to testify that Dr. Chen's testing protocol was flawed in that it dosed the rats at such a level that acid secretion was largely inhibited for the entire testing period and,

therefore, did not allow acid secretion to resume as the drug wore off. Id. (Carlsson) at 8.152:5-18. Additionally, Dr. Carlsson identified inconsistencies in Dr. Chen's testimony regarding control groups. Specifically, on direct examination Dr. Chen testified that control groups were important, yet he stated, without explanation, that he did not include control groups in the testing at issue. Id. (Carlsson) at 8.159:15-20; 8.161:3-10.

The Court, therefore, finds that Dr. Chen's testimony does not meet the requisite standard of clear and convincing evidence. Takeda, 492 F.3d at 1355.

ii. Reason to Modify

The Court finds that Defendant also failed to prove by clear and convincing evidence that a person of ordinary skill in the art would have had a reason to modify Compound 4 to arrive at pantoprazole.

In support of this element, Defendant presented the testimony of Dr. Press. On direct examination, Dr. Press stated that a person skilled in the art would "want" to change the methyls on Compound 4 to hydrogens. Tr. (Press) at 6.98:3-7. However, on cross-examination, he testified that he was not providing any opinion on whether there was motivation to modify Compound 4. Id. (Press) at 6.178:22-179:3. Subsequently, on redirect, he testified that he was mistaken in giving that testimony on cross examination. Id. (Press) at 7.53:17-54:10. The Court finds Dr. Press's testimony inconsistent and unpersuasive. The Court, therefore, finds that Dr. Press's testimony does not meet the requisite standard of clear and convincing evidence. Takeda, 492 F.3d at 1355.

The Court also finds Dr. Press's testimony unpersuasive as to the reason to modify. Dr. Press testified that a person of ordinary skill would not have expected removing the methyls from Compound 4 to result in a compound having improved properties. Id. (Press) at 6.179:4-18.

Accordingly, no reason to modify can be found from an expectation that the new compound would have improved properties. In fact, the effect of making two changes to Compound 4 (i.e., removing a methyl from both the 4 and 6 positions) would be unpredictable. The Court finds that such unpredictability would preclude any expectation that the resulting compound would have favorable properties. Id. (Hopfinger) at 9.189:21-190:20. Thus, no reason was shown why a person skilled in the art would have had a reason to modify Compound 4.

iii. Reasonable expectation of success.

Defendants failed to prove by clear and convincing evidence that a person of ordinary skill in the art would have reasonably expected success in modifying Compound 4 to arrive at pantoprazole. Here, again, Defendant relied exclusively on the testimony of Dr. Press whose testimony depended on the premise that methyls and hydrogens were functionally equivalent substituents. However, on cross examination, Dr. Press was unable cite to specific examples supporting his testimony that methyls and hydrogens were functionally equivalent substituents, i.e., that interchanging methyls and hydrogens would have little or no effect on the potency of the compound. Id. (Press) at 6.184:12-17. In contrast, Plaintiffs presented credible evidence that interchanging hydrogens or methyls at a particular position to compounds in the prior art produced different, and random, potencies depending on whether the compound included hydrogens or methyls at a particular position. Id. (Hopfinger). at 9.190:8-201:19; 10.21:11-29:6.

Accordingly, the Court finds that the weight of credible evidence presented does not establish that hydrogens and methyls are functionally equivalent or functionally interchangeable on PPIs. Therefore, the Court finds that a person skilled in the art would have had no expectation that removing the methyl groups from the 4 and 6 positions of Compound 4 would lead to a compound having the properties of Compound 4 or of pantoprazole.

iv. Objective indicia of non-obviousness

For the reasons set forth above, the Court finds that Plaintiffs have shown the following secondary considerations of non-obviousness: copying and acceptance of others as shown by licensing.

For this reason, the Court finds that Defendant has failed to demonstrate by clear and convincing evidence that Pantoprazole and Compound 4 of the '230 patent are not patentably distinct.

IV. CONCLUSION

For the foregoing reasons, the Court concludes that the Defendant has not demonstrated by clear and convincing evidence that the asserted claims of the '579 patent are invalid either for obviousness under 35 U.S.C. § 103 or under the judicially created doctrine of obviousness-type double patenting. An appropriate final order and judgment accompanies this opinion.

DATED: July 15, 2010

/s/ Jose L. Linares
United States District Judge